REMARKS

The specification has been amended to recite the subject matter of claim 40 as originally filed. No new matter has been added.

Claims 62, 63, 65, 66, 68, 69, 89-103, 105-112, 114, 116, 117, 119, 121-128, and 142-192 were pending in this application before entry of the amendments made herein. Claims 124-126, 169-178 and 192 have been withdrawn by the Examiner as being drawn to non-elected inventions.

Applicant has amended claims 62, 179, and 192 to clarify the claimed invention. Specifically, claims 62, 179, and 192 have been amended to recite a composition comprising an isolated Tat protein, fragment or mutant in combination with a *pharmaceutically acceptable carrier or excipient*, and wherein said composition *is pharmaceutically acceptable for administration to a human.* Support for the amendments can be found in the specification at, *inter alia*, claims 40 and 57 as originally filed, and page 10, lines 15-16 and 30-31.

No new matter has been added. Upon entry of the present amendments, claims 62, 63, 65, 66, 68, 69, 89-103, 105-112, 114, 116, 117, 119, 121-128, and 142-192 will be pending in the present application.

I. STATEMENT OF SUBSTANCE OF INTERVIEW UNDER 37 C.F.R. § 1.133

Pursuant to 37 C.F.R. § 1.133 and MPEP 713.04, Applicant submits this Statement of Substance of Interview in connection with the telephonic interview of June 9, 2006 between Examiner Jeffrey Stucker and Applicant's representative Ann Chen in connection with the above-identified application.

Applicant filed an Applicant Initiated Interview Request Form (PTOL-413A) on June 2, 2006. On June 9, 2006, Applicant's representative Ann Chen was informed by the Examiner that an interview would not be granted at this time. In response, Applicant's representative informed the Examiner that Applicant was willing to file a Request for Continued Examination and a new interview request. The Examiner indicated that an interview would be granted if the Request for Continued Examination and new interview request were properly filed.

Accordingly, Applicant submits herewith a Request for Continued Examination (RCE) Transmittal and an Applicant Initiated Interview Request Form (PTOL-413A).

Applicant respectfully requests that an interview prior to any subsequent Office Action be granted in accordance with 37 C.F.R. § 1.133(a)(2).

II. INFORMATION DISCLOSURE STATEMENT

Pursuant to the Examiner's request, Applicant submits herewith a replacement copy of the form 1449 originally filed on November 17, 2000, listing the same references as originally listed. Applicant submits that the replacement form 1449 properly identifies each publication listed by publisher, author, title, relevant pages of the publication, date and place of publication, and thus, is believed to be in compliance with 37 C.F.R. § 1.98(b)(5). Consideration and entry of the replacement form 1449, as well as return of an Examiner-initialed copy of the replacement form 1449, are respectfully requested.

III. THE CLAIM REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

The rejection of claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 106, 107, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, and 186 under 35 U.S.C. § 102(b) ("Section 102(b)") as allegedly being anticipated by Chang *et al.* (AIDS. 1997 Oct;11(12):1421-31, "Chang") is maintained by the Examiner. Specifically, the Examiner alleges that the Declaration of Shayne Gad, Ph.D. Under 37 C.F.R. § 1.132 ("the First Gad Declaration") and the Declaration of Barbara Ensoli, M.D., Ph.D. Under 37 C.F.R. § 1.132 ("the Ensoli Declaration"), both submitted on December 13, 2005, are not convincing because they are based on opinion and speculation, particularly when such information is within direct knowledge of the inventor/declarant. The Examiner also alleges that even if there were a convincing showing that acetonitrile, trifluoroacetic acid (TFA), etc. were indeed in the final composition obtained by the methods of Chang, Applicant's standard for "suitable for human administration" is the standard of agencies such as the Food and Drug Administration (FDA) or the European Agency for the Evaluation of Medicinal Products (EMEA), and is not the standard for the United States Patent and Trademark Office. For the following reasons, Applicant respectfully disagrees.

1. The Legal Standard

a. Claim Construction

During patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. *In re Hyatt*, 211 F.3d 1367, 1372,

54 U.S.P.Q.2d 1664, 1667 (Fed. Cir. 2000). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 U.S.P.Q.2d 1464, 1468 (Fed. Cir. 1999). The words of a claim must be given their "plain meaning" unless they are defined in the specification. *In re Zletz*, 893 F.2d 319, 321, 13 U.S.P.Q.2d 1320, 1322 (Fed. Cir. 1989); *Chef American, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1372, 69 U.S.P.Q.2d 1857 (Fed. Cir. 2004). "Plain meaning" refers to the ordinary and customary meaning given to a claim term by those of ordinary skill in the art. *See* MPEP § 2111.01. The ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, *i.e.*, as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, U.S.P.Q.2d 1321 (Fed. Cir. 2005) (*en banc*); *Sunrace Roots Enter. Co. v. SRAM Corp.*, 336 F.3d 1298, 1302, 67 U.S.P.Q.2d 1438, 1441 (Fed. Cir. 2003); *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298, 67 U.S.P.Q.2d 1132, 1136 (Fed. Cir. 2003) ("In the absence of an express intent to impart a novel meaning to the claim terms, the words are presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art.").

While less significant than the intrinsic record consisting of the claim language, the specification and prosecution history, extrinsic evidence such as dictionaries are among the many tools that can help determine the meaning of particular terminology to those of skill in the art of the invention. *Phillips v. AWH Corp.*, 415 F.3d at 1317. Extrinsic evidence in the form of expert testimony can be used to establish that a particular term in a patent or the prior art has particular meaning in the pertinent field. *Phillips v. AWH Corp.*, 415 F.3d at 1318.

b. Anticipation

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. *W.L. Gore Associates v. Garlock, Inc.*, 721 F.2d 1540, 1554 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 851 (1984); *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). To anticipate a patent claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. *MEHL/Biophile International Corp. v. Milgraum*, 192 F.3d 1362 (Fed. Cir. 1999); *In re Robertson*, 169 F.3d 743 (Fed. Cir. 1999). It is well established that in order for a prior art reference to amount to an inherent

anticipation of a claim, all the elements of the claim must *necessarily*, *inevitably*, and *always* result from the prior art disclosure and would be so recognized by one of ordinary skill in the art; mere possibilities or probabilities are not sufficient. *See Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d at 1553-54; *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 325-26 (C.C.P.A. 1981); *Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F.Supp. 1278, 1295 n.12, 6 U.S.P.Q.2d 1065, 1076-77 n.12 (D. Del. 1987), *aff'd*, 865 F.2d 1247, 9 U.S.P.Q.2d 1461 (Fed. Cir. 1989); *Hughes Aircraft Co. v. U.S.*, 8 U.S.P.Q.2d 1580, 1583 (Ct. Cl. 1988); *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1463-64 (B.P.A.I. 1990); *Ex parte Skinner*, 2 U.S.P.Q.2d 1788, 1788-89 (B.P.A.I. 1987). As stated by the Court of Appeals for the Federal Circuit:

> we are not persuaded that the 'effect' of the processes disclosed in [the prior art patents], an 'effect' undisclosed in those patents, would be always to inherently produce or be seen always to produce products meeting all of the claim limitations. Anticipation of inventions set forth in product claims cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.

W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d at 1554, citing *In re Felton*, 484 F.2d 495, 500, 179 U.S.P.Q. 295, 298 (C.C.P.A. 1973)).

2. <u>The Meaning of the Claims as Amended</u>

Among the rejected claims, claims 62 and 179 have been amended herein to specify that in the claimed composition, the isolated Tat protein, fragment or mutant is in combination with a pharmaceutically acceptable carrier or excipient, and that the composition *is pharmaceutically acceptable for administration to a human.* The specification does not define the phrase "pharmaceutically acceptable for administration to a human." Thus, the term is given its broadest reasonable interpretation consistent with the interpretation that those skilled in the art would reach. *See In re Hyatt*, 211 F.3d at 1372; and *In re Cortright*, 165 F.3d at 1359. In determining such an interpretation, extrinsic sources such as dictionaries and expert testimony can be used. *See Phillips v. AWH Corp.*, 415 F.3d at 1317-1318. The Federal Circuit has held that extrinsic evidence such as dictionary and expert testimony can be used to establish that a particular claim term has particular meaning in the pertinent field. *See id.*

The Examiner's attention is respectfully directed to Exhibit 1, page 1340 of the Stedman's Medical Dictionary, which defines the term "pharmaceutical" as "[r]elating to pharmacy or to pharmaceutics;" page 1341 of the Stedman's Medical Dictionary, which defines the term "pharmacy" as "[t]he practice of preparing and dispensing drugs," or a "drugstore;" and page 522 of the Stedman's Medical Dictionary, which defines the term "drug" as a "[t]herapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease." These terms are defined in a similar manner in the American Heritage College Dictionary (see Exhibit 2), with the term "drug" being additionally defined as "a substance as recognized or defined by the U.S. Food, Drug, and Cosmetic Act." Applicant submits that the skilled artisan, at the time of the invention, would understand that the phrase "pharmaceutically acceptable for administration to a human" when describing a composition means that the composition is sufficiently safe for administration to human patients such that it can be dispensed and sold as a drug, and thus it must meet the criteria for safety defined by regulatory agencies such as the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA); *i.e.*, the composition does not contain ingredients that the skilled artisan would know, based on knowledge common in the art, would result in denial of regulatory approval for marketing as a drug for humans.

The Examiner's attention is also respectfully directed to the Second Declaration of Shayne Gad, Ph.D. Under 37 C.F.R. § 1.132 ("the Second Gad Declaration") submitted herewith, wherein Dr. Gad states that, in his opinion, as an expert in toxicology and issues relating to development and approval of pharmaceutical products, the phrase "pharmaceutically acceptable for administration to a human" when describing a composition means that the composition is sufficiently safe for administration to human patients using the criteria for safety defined by regulatory agencies such as the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA); *i.e.*, the composition does not contain ingredients that the skilled artisan would know, based on knowledge common in the art, would result in denial of regulatory approval for marketing as a drug for humans. *See* Second Gad Declaration, ¶2. As such, the skilled artisan, at the time of the invention, would understand that the ordinary and customary meaning of the phrase "pharmaceutically acceptable for administration to a human" requires the composition to meet the safety criteria for human administration put forth by regulatory agencies such as the FDA and EMEA which have the public responsibility for determining whether substances are

pharmaceutically acceptable for human administration, and thus requires that the composition not contain substances which are deemed by such agencies as unacceptable in drugs for human administration.

The Second Gad Declaration shows that acetonitrile, TFA, and phenylmethylsulfonyl fluoride (PMSF) are all commonly known to be very toxic, and that a therapeutic containing TFA and acetonitrile, or containing PMSF, would render the therapeutic unsuitable for regulatory approval for human administration, and thus, such therapeutic would *not* be "pharmaceutically acceptable for administration to a human."

3. The Amended Claims are Not Anticipated by Chang

Applicant respectfully submits that the Examiner has maintained the rejection for anticipation based on a misunderstanding of the applicable law. As explained above, in order to anticipate the claimed subject matter, the case law makes it clear that Chang must either (1) disclose *explicitly* that the resulting Tat composition was "pharmaceutically acceptable for administration to a human," or (2) Chang must disclose *inherently* that the resulting Tat composition was "pharmaceutically acceptable for administration to a human." Under the *inherency* standard for anticipation (see above), Chang's procedures as disclosed must *necessarily*, *inevitably*, and *always* result in a Tat composition that is pharmaceutically acceptable for administration to a human. Thus, in order for Chang to anticipate the claims under the correct legal standard, Chang must *explicitly* state that its procedures produce a Tat composition that is pharmaceutically acceptable for administration to a human, *or* Chang's procedures must *necessarily*, *inevitably*, and *always* produce a Tat composition that is pharmaceutically acceptable for administration to a human.

It is abundantly clear that Chang does not *explicitly* disclose a Tat composition that is pharmaceutically acceptable for administration to a human. Instead, Chang is silent as to the solvent used in the HPLC procedure of the first purification method of Chang (as that method is referred to in the Response filed December 13, 2005), and is silent as to whether the resulting Tat preparation is pharmaceutically acceptable for administration to a human. Silence does not meet the legal standard for *explicit* anticipation. Regarding the second purification method of Chang (as that method is referred to in the Response filed December 13, 2005), this method explicitly states that PMSF is included in the buffers used to obtain and purify the Tat protein; thus, Chang explicitly discloses that the Tat preparation of this second method is *not* pharmaceutically acceptable for administration to a human.

Regarding inherent anticipation, Chang's silence regarding the solvent used in the first purification method can only amount to an inherent anticipation if the first purification method *necessarily*, *inevitably*, and *always* would produce a Tat preparation that is pharmaceutically acceptable for administration to a human. This it does not do. As the Examiner states, one could assert, based on the disclosure of Chang that (1) Chang used acetonitrile as a solvent in the HPLC, or (2) that Chang used a less toxic approach (see Office Action, page 4, last paragraph). The crucial point is that Chang's first purification method does not *necessarily*, *inevitably*, and *always* result in either approach. It is well established that in order for a prior art reference to amount to an inherent anticipation of a claim, all the elements of the claim must *necessarily*, *inevitably*, and *always* result from the prior art disclosure and would be so recognized by one of ordinary skill in the art; mere possibilities or probabilities are not sufficient. *See Continental Can Co. USA v. Monsanto Co.*, 948 F.2d at 1269; *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d at 1553-54; *In re Oelrich*, 666 F.2d at 581; *Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F. Supp. at 1295 n.12; *Hughes Aircraft Co. v. U.S.*, 8 U.S.P.Q.2d at 1583; *Ex parte Levy*, 17 U.S.P.Q.2d at 1463-64; *Ex parte Skinner*, 2 U.S.P.Q.2d at 1788-89. Thus, since acetonitrile *may have been* used, especially since it is a commonly used solvent for HPLC, Chang's disclosure of the first method does not meet the standard for inherent anticipation.

Contrary to the Examiner's statements, Applicant's argument does not rely on the assertion that acetonitrile and TFA must have been used by Chang. Rather, Applicant's point is that acetonitrile and TFA may have been used[1], and thus there is no inherent anticipation.

The Examiner objects to the First Gad Declaration for lack of definite knowledge regarding how the Chang Tat protein was purified. *See* Office Action, paragraph spanning pages 4 and 5. The Examiner also objects to the Ensoli Declaration for lack of definite knowledge as to what solvents were used or in what order the purification steps were performed in the first purification method of Chang. *See* Office Action, paragraph spanning pages 5 and 6. The Examiner further alleges that declarations based on opinion and speculation are not convincing particularly when such information is within direct knowledge of the inventor/declarant. *See* Office Action, page 6, lines 7-10.

[1] Although not relevant to the legal point at issue, Dr. Ensoli has confirmed, based on her actual knowledge of what was used in the experiment, that a buffer containing acetonitrile and TFA was in fact used in the reverse phase HPLC step of the Chang reference (as stated in the last sentence of ¶6 of the Ensoli Declaration).

The Examiner seems to imply that the Declarations should have stated what was definitely used by Chang. However, Applicant respectfully submits that it is irrelevant to the instant rejection whether acetonitrile and TFA were actually used in the first purification method described by Chang. The Declarations are persuasive not because they are evidence of what was actually used in the procedures where Chang is silent, but because they show what *could* have been used and, thereby, show that the production of a Tat preparation that is pharmaceutically acceptable for administration to a human is *not* the inevitable outcome of Chang's disclosure. Because such production is not inevitable, under the applicable case law, Chang's disclosure is not sufficient to inherently anticipate the claims. Specifically, the Ensoli Declaration shows that it is possible that Tat obtained by the first purification method of Chang would include acetonitrile and TFA since one skilled in the art would recognize that HPLC would have been performed after the ion-exchange chromatography, and because acetonitrile and TFA are solvents commonly used in HPLC. *See* Ensoli Declaration, ¶¶4-6.

The second purification method of Chang also cannot inherently anticipate the claims, because, as discussed above, it explicitly provides a Tat protein formulated with PMSF, which renders the Tat preparation *not* pharmaceutically acceptable for administration to a human.

Thus, the Tat proteins obtained by both purification methods disclosed by Chang are neither inherently nor explicitly disclosed by Chang to be pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Therefore, Chang does not teach or suggest each and every element of amended claims 62 and 179, and thus, their respective dependent claims. In particular, Chang does not teach a composition comprising an isolated, biologically active Tat protein, mutant, or fragment that is *pharmaceutically acceptable for administration to a human*, as recited in amended claims 62 and 179.

Thus, Applicant submits that claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 106, 107, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, and 186, all of which require that the Tat composition comprise a pharmaceutically acceptable carrier or excipient and that it be pharmaceutically acceptable for administration to a human, are novel over Chang. Withdrawal of the Section 102(b) rejection is respectfully requested.

IV. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103 ARE IN ERROR AND SHOULD BE WITHDRAWN

1. The Claims Are Patentable Over Chang in View of Heiman

The rejection of claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 106, 107, 114, 119, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, 186, and 189 under 35 U.S.C. § 103(a) ("Section 103(a)") as allegedly being obvious over Chang in view of the web pages entitled "HIV Vaccines: Where are we Going?" (http://www.niaid.nih.gov/daids/vaccine/1998nature.htm, "Heiman") is maintained by the Examiner. Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." *Hartness International Inc. v. Simplimatic Engineering Co.*, 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987).

Further, an obviousness rejection cannot be based on inherent disclosure in a prior art reference. The Court of Customs and Patent Appeals has stated that "the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966).

The deficiencies in the teaching of Chang are discussed above. There is no suggestion in Chang of a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein the composition is *pharmaceutically acceptable for administration to a human*, as recited in

amended claims 62 and 179. There is no explicit suggestion of the foregoing in Chang, and silence of Chang regarding the first purification method is not a suggestion. Chang's silence as to the HPLC solvents used in the first purification method cannot be used as a basis for the Section 103(a) rejection, since "obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d at 448. The skilled artisan would not recognize Chang as teaching or suggesting a Tat preparation that is pharmaceutically acceptable for administration to a human. The second purification method of Chang, as discussed above, produces a Tat preparation containing PMSF, clearly rendering it *not* pharmaceutically acceptable for administration to a human, and there is no suggestion in Chang to avoid the use of PMSF.

Heiman does not cure the deficiency of Chang, because Heiman also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a human; thus, Heiman does not provide the missing suggestion. Accordingly, the combination of Chang plus Heiman does not teach or suggest the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

2. <u>The Claims Are Patentable Over Chang in View of Vogel</u>

The rejection of claims 62, 63, 65, 66, 68, 69, 89, 90, 93-95, 97, 101-103, 105-111, 116, 117, 121, 122, 128, 142-168, 179-187, 190, and 191 under Section 103(a) as allegedly being obvious over Chang in view of Vogel *et al.* (Vogel FR, Powell MF. 1995. A compendium of vaccine adjuvants and excipients. In: Powell MF, Newman MJ, editors. Vaccine design: The Subunit and Adjuvant Approach. Plenum, New York, "Vogel") is maintained by the Examiner. Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

As discussed above, Chang does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein said composition is pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Vogel does not cure the deficiency of Chang, because Vogel also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a

human; thus, Vogel does not provide the missing suggestion. Accordingly, the combination of Chang plus Vogel does not teach or suggest the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

3. The Claims Are Patentable Over Chang in View of Castignolles

The rejection of claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 99, 106, 107, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, and 186 under Section 103(a) as allegedly being obvious over Chang in view of Castignolles *et al.* (Vaccine. 1996 Oct;14(14):1353-60, "Castignolles") is maintained by the Examiner. Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

As discussed above, Chang does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein said composition is pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Castignolles does not cure the deficiency of Chang, because Castignolles also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a human; thus, Castignolles does not provide the missing suggestion. Accordingly, the combination of Chang plus Castignolles does not teach or suggest the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

4. The Claims Are Patentable Over Chang in View of Ramshaw

The rejection of claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 100, 106, 107, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, and 186 under Section 103(a) as allegedly being obvious over Chang in view of Ramshaw *et al.* (J Immunol Methods. 1977;18(3-4):251-5, "Ramshaw") is maintained by the Examiner. Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

As discussed above, Chang does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein said composition is pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Ramshaw does not cure the deficiency of Chang, because Ramshaw also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a human; thus, Ramshaw does not provide the missing suggestion. Accordingly, the combination of Chang plus Ramshaw does not teach or suggest the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

5. The Claims Are Patentable Over Chang in View of Livingston

Claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 106, 107, 112, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, 186, and 188 are rejected under Section 103(a) as allegedly being obvious over Chang in view of Livingston *et al.* (J Immunol. 1997 Aug 1;159(3):1383-92, "Livingston"). Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

As discussed above, Chang does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein said composition is pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Livingston does not cure the deficiency of Chang, because Livingston also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a human; thus, Livingston does not provide the missing suggestion. Accordingly, the combination of Chang plus Livingston does not teach or suggest the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

6. The Claims Are Patentable Over Chang in View of Barry

Claims 62, 63, 65, 66, 68, 69, 89, 90, 93, 94, 106, 107, 123, 128, 142-150, 152, 153, 155-159, 161, 162, 164-168, 179-183, 185, and 186 are rejected under Section 103(a) as allegedly being obvious over Chang in view of Barry *et al.* (Clin Pharmacokinet. 1997 Mar;32(3):194-209, "Barry"). Specifically, the Examiner alleges that Applicant's prior arguments concerning Chang are not convincing and the rejection is maintained.

As discussed above, Chang does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, wherein said composition is pharmaceutically acceptable for administration to a human, as recited in amended claims 62 and 179. Barry does not cure the deficiency of Chang, because Barry also does not teach or suggest a composition comprising an isolated Tat protein, fragment or mutant in combination with a pharmaceutically acceptable carrier or excipient, that is pharmaceutically acceptable for administration to a human; thus, Barry does not provide the missing suggestion. Accordingly, the combination of Chang plus Barry does not teach or suggest the presently claimed invention.

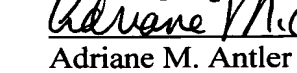
In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

CONCLUSION

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: June 14, 2006



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